

Lecture 10. Glycomics.

Learning outcomes:

1. Give the definitions to the following terms: “carbohydrates”, “monosacharids”, “disacharids”, “polysacharids”, “glycome” and “glycomics”, give the specific examples.
2. Analyze the chemical structure and fuctions of different carbohydrates, give the specific examples.
3. Describe the chemical structure and function of glycoproteins and proteoglycans.
4. Explain how some glycoproteins (lectins) can participate in cellular recognizing, adhesion and interactions between the cells (so called “sugar code”)?
5. Explain different disturbances of carbohydrate metabolism and methods of their diagnostics and treatment, give the specific examples.

Glycomics is the comprehensive study of **glycomes** (the **entire complement of sugars**, whether free or present in more complex molecules of an organism), including genetic, physiologic, pathologic, and other aspects. Glycomics "is the systematic study of all **glycan structures** of a given cell type or organism" and is a subset of glycobiology. The term glycomics is derived from the chemical prefix for sweetness or a sugar, "glyco-", and was formed to follow the omics naming convention established by genomics (which deals with genes) and proteomics (which deals with proteins).

Challenges for glycomics:

- The **complexity of sugars**: regarding their structures, they are not linear instead they are highly branched. Moreover, glycans can be modified (modified sugars), this increases its complexity.
- Complex **biosynthetic pathways** for glycans.
- Usually **glycans** are found either bound to protein (glycoprotein) or conjugated with lipids (glycolipids).
- Unlike genomes, **glycans** are highly dynamic.

This area of research has to deal with an inherent level of complexity not seen in other areas of applied biology. **68 building blocks** (molecules for DNA, RNA and proteins; categories for lipids; types of sugar linkages for saccharides) provide the **structural basis** for the molecular choreography that constitutes the entire life of a cell. DNA and RNA have four building blocks each (the nucleosides or nucleotides). Lipids are divided into eight categories based on ketoacyl and isoprene. Proteins have 20 (the amino acids). **Saccharides have 32 types of sugar linkages**. While these building blocks can be attached only linearly for proteins and genes, they can be arranged in a branched array for saccharides, further increasing the degree of complexity.

Add to this the complexity of the numerous proteins involved, not only as carriers of carbohydrate, the **glycoproteins**, but proteins specifically involved in binding and reacting with carbohydrate:

- **Carbohydrate-specific enzymes** for synthesis, modulation, and degradation
- **Lectins**, carbohydrate-binding proteins of all sorts
- **Receptors**, circulating or membrane-bound carbohydrate-binding receptors

Importance of glycomics:

- Glycoproteins and Glycolipids found on the cell surface play a critical role in bacterial and viral recognition.
- They are involved in cellular signaling pathways and modulate cell function.
- They are important in innate immunity.
- They determine cancer development.
- They orchestrate the cellular fate, inhibit proliferation, regulate circulation and invasion.
- They affect the stability and folding of proteins.
- They affect the pathway and fate of glycoproteins.

- There are many glycan-specific diseases, often hereditary diseases.

There are important medical applications of aspects of glycomics:

- **Lectins** fractionate cells to avoid graft-versus-host disease in hematopoietic stem cell transplantation.
- Activation and expansion of cytolytic **CD8 T cells** in cancer treatment.

Glycomics is particularly important in **microbiology** because **glycans** play diverse roles in **bacterial physiology**. Research in bacterial glycomics could lead to the development of:

- **novel drugs**
- **bioactive glycans**
- **glycoconjugate vaccines**

High-resolution mass spectrometry (MS) and high-performance liquid chromatography (HPLC), Multiple Reaction Monitoring (MRM), metabolic and covalent labeling of glycans, X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, chromatography (affinity chromatography etc.) and analytical electrophoresis (PAGE (polyacrylamide electrophoresis), capillary electrophoresis, affinity electrophoresis are examples of the commonly used techniques in glycan analysis.

The questions for self - control:

1. What are the “carbohydrates”, “monosacharids”, “disacharids”, “polysacharids”, “glycome” and “glycomics”?
2. Chemical structure and fuctions of different types of carbohydrates, glycoproteins and proteoglycans.
3. Diseases connected with the disturbances of carbohydrate metabolism and methods of their diagnostics and treatment.

Recommended readings:

1. Rudd, P; Karlsson, NG; Khoo, KH; Packer, NH; Varki, A; Cummings, RD; Esko, JD; Stanley, P; Hart, GW; Aebi, M; Darvill, AG; Kinoshita, T; Packer, NH; Prestegard, JH; Schnaar, RL; Seeberger, PH (2015). "Glycomics and Glycoproteomics". doi:10.1101/glycobiology.3e.051 (inactive 2021-01-18). PMID 28876822.
2. Aoki-Kinoshita KF; Lewitter, Fran (May 2008). Lewitter, Fran (ed.). "An Introduction to Bioinformatics for Glycomics Research". PLOS Comput. Biol. 4 (5): e1000075. Bibcode:2008PLSCB...4E0075A. doi:10.1371/journal.pcbi.1000075. PMC 2398734. PMID 18516240.
3. Srivastava S (May 2008). "Move over proteomics, here comes glycomics". J. Proteome Res. 7 (5): 1799. doi:10.1021/pr083696k. PMID 18509903.
4. Essentials of Glycobiology (2nd ed.). Cold Spring Harbor Laboratory Press. 2009. ISBN 978-087969770-9.
5. Aizpurua-Olaizola, O.; Toraño, J. Sastre; Falcon-Perez, J.M.; Williams, C.; Reichardt, N.; Boons, G.-J. (2018). "Mass spectrometry for glycan biomarker discovery". TrAC Trends in Analytical Chemistry. 100: 7–14. doi:10.1016/j.trac.2017.12.015.
6. ucsd news article Do 68 Molecules Hold the Key to Understanding Disease? published September 3, 2008
7. Reid, CW; Twine, SM; Reid, AN (editor) (2012). Bacterial Glycomics: Current Research, Technology and Applications. Caister Academic Press. ISBN 978-1-904455-95-0.